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The Classic

The Treatment of Malignant Tumors by Repeated Inoculations of Erysipelas

With a Report of Ten Original Cases

WILLIAM B. COLEY, M.D.

William Bradley Coley (Fig. 1) stemmed from old New England stock. After graduating from Yale in 1884, Coley spent two years in Portland, Oregon, teaching Latin and Greek before entering Harvard Medical School. After completing a competitive examination, he became an intern at the New York Hospital in the service of Drs. Weir and Bull. It was one of Dr. Bull's patients who stimulated Coley's interest in the treatment of sarcomas and advanced cancers. The patient had a recurrent sarcoma of the cervical region that disappeared after an erysipelas infection in the region of the wound. Coley began inoculating patients with inoperable tumors in an attempt to produce erysipelas. With Dr. Bull's support, Coley was able to pursue this work at the New York Cancer Hospital (now the Memorial Sloan–Kettering Cancer Center). One of Coley's patients donated $100,000 to establish the C. P. Huntington Fund for Cancer Research, the first cancer research fund in the United States. Coley remained associated with this hospital for more than 40 years. As a result of his experiments, Coley developed a preparation consisting of killed cultures of *Streptococci* and *Bacillus prodigiosus*. This became known as Coley's toxins and was widely used in treating patients with sarcomas, occasionally with success. His son, Bradley L. Coley, continued work on the treatment of bone tumors. In addition to his interest in the treatment of tumors, Coley was well known for his work on the treatment of inguinal hernia and was the first surgeon in the United States to adopt the Bassini method of repair. He was on the staff of the Hospital for the Ruptured and the Crippled for many years and served as chief surgeon for the last seven years before retiring in 1932. William Bradley Coley was a pioneer in the immunologic approach to the treatment of malignant disease. His career can be summed up in the citation read at the time he received the degree of Honorary Master of Arts from Harvard University in 1911: "William Bradley Coley, surgeon, medical discoverer, and director of medical research; who learned to cure by surgery ills that foiled its art, and without surgery, others beyond its reach."

LEONARD F. PELTIER, M.D.

In a paper published in the *Annals of Surgery*, in September 1891, entitled "A Contribution to the Knowledge of Sarcoma," I referred at some length to the curative effect of erysipelas upon sarcoma, reporting the results of inoculation in three cases recently treated by myself.

At the time I began my investigations in this most interesting subject, I had not read of Fehleisen's experiments in Germany. While collecting the cases of sarcoma treated at the New York Hospital during the past fifteen years, I found a case that, to my mind, had

Abridged from Coley, W.B.: The treatment of malignant tumors by repeated inoculations of erysipelas: With a report of ten original cases. Am. J. Med. Sci. 105:487. 1893.

FIG. 1. William Bradley Coley (1862–1936).

convincing evidence that erysipelas possessed a powerful curative principle antagonistic to sarcoma.

Whether or not this principle could be isolated or utilized in the practical treatment of sarcoma was quite another question, yet one of sufficient interest and importance to lead me at once into making a thorough study of the subject.

Before going further it might be well to give a few points of interest in the case I have mentioned:

This was one of round-celled sarcoma of the neck, occurring in a German, aged thirty-one years. Five operations had been performed by Dr. W. T. Bull within a space of three years. At the last operation it was found impossible to remove all of the tumor, and the case was considered hopeless.

Two weeks after the operation a severe attack of erysipelas occurred, followed by a second attack shortly after the first had subsided.

During the progress of the erysipelas the remains of the sarcoma entirely disappeared, the wound rapidly healed, and the patient was seen both by Dr. Bull and myself seven years afterward, at which time the photograph appended was taken.

The diagnosis in this case had been repeatedly confirmed by well-known pathologists, and there was no possibility of attributing the cure to any other cause than the erysipelas.

If erysipelas, a disease produced by a specific organism, could cure a case of undoubted sarcoma when occurring accidentally, it seemed fair to presume that the same benign action would be exerted in a similar case if erysipelas could be artificially produced.

Was it possible to produce an artificial erysipelas, and if so, what were its dangers and limitations? These were questions that immediately arose, and the answers to them, crude and imperfect though they be, I shall now endeavor to present.

In the course of a careful review of the literature of the subject, I found that, aside from a vague and indefinite impression that tumors of doubtful character had been known to disappear after an attack of erysipelas, there was a certain amount of actual evidence. This evidence, though made up of facts few in number and scattered, was nevertheless strong.

It was made infinitely stronger by the publication of Fehleisen's paper in 1883, demonstrating the origin of erysipelas from a specific germ, and giving the results of a series of experiments upon five cases of malignant disease.

Having satisfied myself that the mortality from erysipelas uncomplicated was very small, I determined to inoculate the first case of inoperable sarcoma that should present itself.

I had but a short time to wait, and on May 2, 1891, I inoculated a case of sarcoma of the neck and tonsil (recurrent), which was kindly referred to me by Dr. Bull:

The patient was an Italian, thirty-five years of age, operated on previously in Rome by Professor Durante, and in April 1891, by Dr. Bull, at the New York Hospital. At the latter operation the growth was found too extensive

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to remove. At the time of my first inoculation, the tumor of the neck was growing, and the right tonsil was the seat of a tumor the size of a hen's egg and almost completely blocking the pharynx. Solid food could not be taken, and liquids frequently regurgitated through the nose.

The patient's condition was very bad. He was emaciated and cachectic. The dangers attendant upon an attack of erysipelas were explained to him, and in view of the hopelessness of his condition and the impossibility of obtaining further surgical relief, he consented to erysipelas inoculation.

The details of the earlier treatment are given in my former paper, and I will not repeat them here; suffice it to say that the inoculations were made by injecting small quantities of bouillon cultures (1/2 to 2 grammes) into the tumor itself, scarification (Fehleisen's method) having proved unsatisfactory.

The inoculations were continued at short intervals during May and part of June. Slight local and constitutional reaction followed the inoculations, the tumor of the neck diminished in size, and the general condition improved. The tonsil tumor was also smaller and the voice much better.

During August and September, the treatment was discontinued, and the tumors at once began to increase in size and the general condition to deteriorate.

By October 1st they had reached their former size, and the patient's condition was little different from that at the time the inoculations were begun. At this time I succeeded in getting a culture of streptococcus erysipelatis kindly brought to me by Dr. Farquhar Ferguson, direct from Koch's laboratory, and I decided to make a further trial.

Five decigrammes of a fresh culture were injected into the tumor substance. Up to this time he had had no attack of true erysipelas, the slight local reaction passing away in from twenty-four to forty-eight hours, and the temperature thereupon becoming normal.

Within an hour he had severe pain, nausea, vomiting, and a chill lasting forty minutes. His temperature rose to 105°, and within twelve hours a patch of perfectly typical erysipelas the size of the palm of the hand appeared on the neck. This gradually extended over the face and head, and met upon the opposite side.

The disease ran the usual course, and I made little effort to check it, save to apply some ichthyol on the forehead to prevent its extending to the scalp (which, I may add, it failed to do). At the end of ten days, the pulse and temperature had become normal. The tumor of the neck began to break down on the second day, and discharged until the end of the attack. The discharge was not pus, but resembled the caseous material of a tubercular gland. The outlying nodules disappeared by absorption without breaking down. The tonsil tumor was smaller, but the diminution in size was not great. At the end of two weeks the tumor of the neck had disappeared, and there remained only the induration from the previous operations.

The appetite soon began to improve, and he gained rapidly in flesh and strength. There has been up to the present time (twenty months) no return of the tumor in the neck, and although the tonsil tumor has remained about the same in size, its malignant character must have been greatly modified, as sarcoma of the tonsil is known to be rapidly fatal.

The patient's general condition at present (nearly two years) is very good, although he is suffering from a confirmed morphine habit that he had contracted previous to the inoculations.

My second and third cases were bone sarcomata (periosteal), one of the lower end of the femur and the other of the upper dorsal spine. These two cases are, as far as I have been able to ascertain, the only cases of bone tumors where inoculation has been tried; although Dr. Gerster reported at the Surgical Society, a year ago, a most remarkable case of sarcoma of the lower end of the femur, with

amputation at the trochanter minor, followed by rapid recurrence in the stump. An attack of accidental erysipelas ensued a few weeks later, whereupon the tumor entirely disappeared, and the patient was seen by Dr. Gerster three years afterward, free from recurrence.

The results in my two cases, although temporarily beneficial, were not successful from a curative point of view. It is worthy of note, however, that in neither case was erysipelas obtained. The reaction, both local and constitutional, resembled exactly that which occurred in the early treatment of the first case; and the slight improvement compared with what I have observed after true attacks of erysipelas, has led me to regard the presence of the streptococci themselves as a very important factor in destroying the neoplasm. My own experiments in the use of sterilized cultures of erysipelas, as well as the recent researches of Stronck, still further confirm this view.

In addition to these cases of my own, I have collected and tabulated all the reported cases of carcinoma and sarcoma in which erysipelas, either spontaneous or artificial, intervened. It is from careful study and analysis of these cases, as well as from the more practical experience derived from my own cases, that my conclusions are based.

Time will not permit me to go into these cases in detail, and I can do nothing more than give a brief summary of the results.

We find a total of 38 cases of malignant disease in which an erysipelas has occurred, either by accident or intent.

Of these 38 cases the erysipelas occurred accidentally in 23 cases, and was the result of inoculation in 15 cases (including my own): 17 cases were carcinoma, 17 cases were sarcoma, and 4 either sarcoma or carcinoma.

The immediate and final results were as follows:

Carcinoma. Of the 17 cases, 3 were permanently cured. In addition, 1 case of probable carcinoma (Hutchinson's) was well five years after the attack of erysipelas. Of the remaining 13, 10 showed improvement, which, although temporary, undoubtedly added to the life of the patient in most cases. One case (Janike's) died, as a result of the erysipelas, on the fourth day.

Sarcoma. In turning to sarcoma we find the curative action of the erysipelas even more marked. Of the 17 cases of sarcoma, we find 7, or 41 %, well and free from recurrence from one to seven years after the attack of erysipelas. Nearly all of these 7 cases have a remarkable history. The cases of Dr. Bull, Dr. Gerster, and my own have already been described.

The remaining 4 were as follows: The first (Biedert's) was a very large round-celled sarcoma, involving mouth, face, nose, and orbit of a child ten years of age. The features were greatly distorted, and the general condition so bad that death from exhaustion was anticipated soon. While in daily expectation of being obliged to do a tracheotomy, a severe attack of facial erysipelas occurred. The tumor disappeared, as if by magic, during the course of the erysipelas. The child recovered, and at the end of a year was perfectly well, with no trace whatever of recurrence.

The next case (Brun's) was a melanotic sarcoma of the breast, with entire disappearance, and no recurrence.

The sixth case (Busch's) was a multiple sarcoma of the face that entirely disappeared after an attack of facial erysipelas, and did not return.

The seventh case (Kleeblatt's) was a lympho-sarcoma of the neck, very large; the erysipelas in this case being the result of inoculation.

In addition to these seven cases, there is one other, a probable sarcoma of the breast, that was cured.

Ten of the remaining eleven showed more or less marked improvement; in some cases the tumor entirely disappearing, and not recurring for several months.

One case died as a probable result of the erysipelas, which was in this instance accidental.

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To put the result still more briefly: In carcinoma, 17 cases, 3 cures, 17.6 %; 1 death, 5.9 %. In sarcoma, 17 cases, 7 cures, 41 %; 1 death, 5.9 %; 4 sarcoma or carcinoma, 2 cured.

These cases have been in no way selected, and I have made every effort to include all cases resting on competent authority, yet it might be urged as an objection to accepting these figures as representing the true percentage of cures, that cases have probably occurred which, owing to no marked improvement following the erysipelas, naturally failed to be reported. This objection, though valid as far as the accidental cases are concerned, would cease to hold in the cases of inoculation for the reason that, being so few in number, all, or nearly all, have probably been reported.

Grouping by themselves, then, the cases where the erysipelas was artificially produced, we find 7 cases of carcinoma, 1 cure, or 14.3 %, and 8 cases of sarcoma, 2 cures, 25 %. These cases were as follows: Fehleisen, 2; Kleeblatt, 2; Busch, 1; the remaining 3 cases being my own.

These figures may then be taken to fairly represent the curative effect on carcinoma and sarcoma in the worst cases; and when we reflect that in nearly every instance the tumor was not a primary growth, amenable to operative treatment, but either a recurrence after operation had been tried and failed, or from its nature inoperable, then and then only are we in a position to fully estimate the importance and value of erysipelas as a *curative* agent.

I have purposely excluded in the foregoing analysis 8 cases of my own treated by *repeated injections* of erysipelas cultures, which, without producing erysipelas, caused marked improvement in the tumors. These cases should be grouped by themselves, and they bring us back to the question regarding the nature of this *curative principle,* which, however variable its action, must be regarded as having a constant relation to erysipelas.

In my former paper I referred briefly to the different theories offered in explanation of this benign action, and even then I was inclined to believe it due to "antagonistic bacterial action," the neoplasm being regarded as dependent on some unknown microorganism.

Since that time the evidence in favor of the microparasitic origin of cancer has been steadily and rapidly accumulating until at the present moment it rests little short of absolute demonstration. Time will not permit more than a brief mention of the more salient points of this evidence, yet since a proper appreciation of its character and strength is necessary to anything like a clear understanding of the probable action of erysipelas on malignant tumors, we cannot pass over it unnoticed. We shall consider the following:

(1) *The close resemblance of cancer to other diseases known to be of bacterial origin.* The striking analogy between cancer and tuberculosis was noticed long before the tubercle bacillus was discovered. Sir John Simon in 1877 clearly pointed out this analogy, and in fact even then argued very strongly in favor of a microparasitic origin of cancer. His paper states the points at issue so clearly and briefly, and moreover, the facts adduced and the conclusions drawn—showing as they do an almost prophetic insight—make it a paper that can be read with the greatest interest and profit today. He pointed out the error in the earlier investigations in allowing the "anatomical forms," interesting enough in themselves, to obscure the more important "property of infectiousness," which he regarded as the "real puzzle" of the disease. "The anatomical forms are matters of mere local accident, but the infectiousness of cancer represents its very cause." He showed that the element of heredity plays an entirely different role in cancerous and noncancerous tumors; that while in the latter the hereditary influence often seems to be the *entire* cause of the tumor, an "embryonic fault" belonging to the same pathological class as supernumerary toes and fingers—in *cancer* it supplies only that portion of the cause which, as in tuberculosis, is

familiarly known as *predisposing conditions.* This opinion we know is generally accepted at the present day. There is, moreover, a growing tendency to no longer adhere to the stereotyped classification of "tumors," and we venture to predict that in the near future, instead of "tumors," a class at present embracing elements without the remotest analogy either in their etiology or mode of development, we shall have two main groups—the first of which might be designated as *congenital hypertrophies;* the second, *neoplasms,* etiologically dependent on infection from without.

This statement may seem a trifle strong, since Cohnheim's embryonic theory of the origin of cancer is not only still held by the larger body of medical men, but has quite recently been championed by Baumgarten in Germany as well as by distinguished pathologists in this country. In spite of all the objections and criticisms, the microparasitic theory has steadily gained ground, and just now the confirmations are rapidly outnumbering the objections. These objections, the most of which were formulated by Cohnheim himself, ten years ago, have nearly all been answered. He argued that cancer could not be of microbic origin, first, because it was neither epidemic nor endemic. Tuberculosis is neither epidemic nor endemic, yet because of Koch's bacillus. Malaria is neither contagious nor epidemic, yet is caused by an intracellular parasite; again, tetanus is not contagious, and hardly more endemic than cancer itself, as shown by the researchers of Haviland, and confirmed by recent investigations.[1] The second objection was that cancer could not be inoculated from one individual to another or to animals.

Cancer has been transferred from one part of the body to others in the same individual (Hahn and Von Bergmann) by inoculation, and moreover, it has been transferred from one animal to others in a few cases. That most of the experiments in inoculating animals have failed is really no objection to the theory. We know that there are many vegetable and animal parasites whose life history embraces a long cycle of changes in form and development, only a brief portion of which is found in the "host."

The *evolution of parasites* is a subject of great interest and importance, yet one that, as yet, has been but little investigated by the trained naturalist and biologist.

For a clearer understanding of the "laws of parasitism," and their relation to specific diseases, we are much indebted to the recent and valuable contribution of Dr. Joseph Frank Payne, of London. If his view, that there is a definite relation between the contagiosity of a specific disease and its chronicity be correct, we at once see a striking analogy between cancer on the one hand, leprosy and tuberculosis on the other, and there is no need to go further for an explanation of the slight contagiosity of cancer. Ballance and Shattuck go so far as to assert that "there is no fact in the etiology or life history of carcinoma or sarcoma that has not its counterpart in tuberculosis."

(2) *Analogous diseases in animals and plants known to be of parasitic origin.* In the vegetable kingdom we find a large variety of "tumors" known as "galls." One by one these have all been proven to be of parasitic origin. If we turn to the lower animals, we find in "coccidial infection" an analogy so striking, that many observers have considered it identical with cancer. Without entering into any discussion of this question, this much may be regarded as proven: That certain low organisms or protozoa known as coccidia have been found in animals, chiefly rabbits; that they possess the very *rare* property of being able to set up a proliferation of epithelium; that in the animals in question, and at least in one case (Leuckhart's) if not in two cases in man, they have produced multiple tumors

[1] Since the above was written, the very valuable researches of Roger have been published in the Revue de Méd., December, 1892. They go far toward proving that the virtue of the erysipelas rests in the toxic products, which can be easily isolated and used in much larger doses than by Spronck.

associated with the same clinical symptoms and pathological changes that are found in true cancer.

We must further admit that several independent observers, notably Sawtschenko on the Continent, and Ruffer and Walker in England, by the use of improved methods of staining, have been able to demonstrate the constant presence of protozoa in a very large number of specimens of carcinoma. That these are true parasites and not "invaginated cells" or "degenerated metamorphoses," as many have been inclined to regard them, has been very recently confirmed by the testimony of Metschnikoff, the highest living authority in microzoology.

These protozoa are so similar to the coccidia already referred to, that they can scarcely be differentiated. Whether or not they are identical, seems to me a matter of indifference; that they are very closely allied forms seems more than probable. That they have not yet been cultivated outside the body is no evidence against their being the cause of cancer, when we consider how much time it has taken to discover their mere presence.

If, with a distinguished authority, we admit that "for the development of cancer it is necessary that there should be a continuous irritation, and one capable of multiplication," and knowing as we do that the irritants capable of fulfilling these conditions are limited almost entirely to the animal and vegetable parasites, we can scarcely fail to accept the microparasitic theory. The great merit of this theory, as Ballance and Shattuck have pointed out, is that "it not only offers a working hypothesis for further investigation with which none other can compare, but it holds out the hope that it may one day admit of scientific treatment based on the same lines as other microparasitic diseases." Having endeavored to make clear the grounds for believing in the parasitic origin of cancer, the explanation of the action of erysipelas is not difficult. If a small quantity of blood-serum of an animal rendered immune to tetanus is capable of destroying or rendering inert the virulent bacilli in a fresh case, it is quite as easy to understand that the toxic products of the erysipelas streptococci might bring about such changes in the bloodserum as to destroy the parasite of cancer. The parasite having been destroyed, the irritation would consequently cease, and this would lessen the hyperæmia of the parts, on which factor the life of the tumor-cells of low vitality largely depends.

This theory, if it may be called such, has occurred to me as offering the best explanation of all the phenomena observed. It explains the rapid degeneration, with a breaking down of the tumor tissue, as well as the slower disappearance by absorption. It also explains those interesting cases, several in number, where an erysipelas remote from the tumor has caused a disappearance in precisely the same way as a local attack. These latter cases, it would seem, prove the phagocytosis theory insufficient to explain the action of erysipelas. It is worthy of note that the action of erysipelas on lupus and the secondary and tertiary lesions of syphilis (see Mauriac) is similar to that in malignant tumors, and this fact, joined to the fact that erysipelas has never been known to affect nonmalignant tumors, is another point in favor of the parasitic origin of cancer.

The attempt to explain its action on the theory of a mere local irritation, classing it with the various caustics, needs only to be mentioned to be disproved.

The clinical facts already mentioned, that a number of malignant tumors have disappeared as a result of an erysipelas in another region of the body, coupled with the very recent experiments of Professor Spronck and his co-workers in Leyden, settle the point beyond dispute. In the experiments referred to, twenty-six cases of malignant disease (eight sarcoma, eighteen carcinoma) were injected subcutaneously with the toxic products of the streptococcus of erysipelas, the germ itself having been destroyed and removed.

In every case the injections were made in parts remote from the tumor, usually the glu-

teal region. Nearly all of the cases of sarcoma showed marked improvement, and in some cases the tumor entirely disappeared. It is true recurrence usually took place, yet in one case (Remsen's), a large inoperable sarcoma, the primary growth entirely disappeared, the secondary growths were reduced to very small size, and there had been no recurrence up to the publication of the paper.

The effect on carcinoma was very slight, and only in one case was the beneficial action marked.

It should be noted that very small doses were used in these cases, one-half to one gramme.

In no case was the reaction very great, 103° being the highest temperature recorded, the condition usually becoming normal at the end of twenty-four hours. Spronck himself admits that better results might have been obtained from larger doses, yet he preferred to err on the side of safety.

Treatment by repeated injections of fluid cultures. As far as I know, my cases are the only ones that have been treated by repeated injections of the pure fluid cultures of erysipelas.

I began this method more than eighteen months ago, and have used it in nearly all my cases. In most cases I have made the injections deeply into the tumors themselves. The doses employed have varied with the age and virulence of the cultures, but I have aimed to obtain a good reaction, a temperature of 104° or 104½° frequently following. The reaction has usually subsided within thirty-six to forty-eight hours after the injection, unless erysipelas was produced. The effect on the tumors was more marked in the cases of sarcoma than carcinoma, but all cases showed a cessation of growth and a more or less marked diminution in size. Several sarcomatous nodules, some nearly one inch in diameter, disappeared entirely. It is evident that in these cases the effects produced were chiefly because of the toxic products of the streptococci.

In view of these results, as well as those of Spronck, it may be considered definitely proven, that a portion, if not all, of the benign influence rests in the toxic products of the erysipelas germ, rather than in the germ itself. The fact that, thus far, the results from an attack of true erysipelas have been far more brilliant and permanent prove that either the germ itself or its continued action plays an important rôle, or, what is quite as probable, we have not yet learned how best to isolate the toxic principles and to use them in the most efficacious doses. It is more than probable that sterilizing cultures by heat changes the chemical relations of the toxalbumins. I am at present, with the assistance of Dr. Alexander Lambert, making experiments with *filtered cultures,* the germs having been removed by means of a Kitasato filter, without subjecting the fluid filtrate to heat. If the virtue of the erysipelas lies entirely in these toxic principles, the treatment of malignant disease will be much simplified, as there will be neither the danger from the erysipelas nor the necessity for isolation.[1]

Dangers associated with erysipelas. I have endeavored to ascertain as far as possible the actual mortality of uncomplicated erysipelas. Nearly everything that has been written upon the subject is of little value in determining this point, because the term "erysipelas" has been used in a very loose way, including many cases of cellulitis and septic infection. I do not believe in the identity of the streptococcus of erysipelas and the streptococcus pyogenes, although I am aware that the opposite opinion is held by many of the leading bacteriologists. Those who hold to the identity of the two germs, base their opinion largely upon the close resemblance, morphologically and biologically, and they claim that the clinical differences are because of the different sites of infection and variations in virulence of cultures; that the same germ in the outer layers of the skin will produce true erysipelas, and that injected deeply into the tissues will cause cellulitis and multiple ab-

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scesses. I believe this explanation entirely theoretical and not supported by facts. During the course of these experiments, I have injected, upward of one hundred fifty times, pure cultures of the streptococcus of erysipelas, of almost every degree of virulence, into the (human) tissues, superficially and deeply. In but two cases did I see an abscess, and in one of them a careful bacteriological examination was made of the pus (before it had become contaminated), and mixed cultures were found, the staphylococcus aureus being present with the streptococcus.

There appears to be good ground for believing that when suppurative processes are associated with erysipelas, a mixed infection is present, and that there is a real and important difference between the germ of erysipelas and the streptococcus pyogenes, in spite of their close resemblance.

The fact that they are pathogenic for different animals, respectively, and also their different action with reference to lactic acid, are other points against their identity.

If we include the cases of diphtheria inoculated with erysipelas (Babtschinski), we have a total of 40 cases where erysipelas has been artificially produced, with but one death—2½%. We know that the virulence of the germ varies within wide limits, and that it can be modified at will by passing it through animals; therefore it seems reasonable to assume that with proper precautions its mortality in inoculation can be made trifling or *nil.*

CONCLUSIONS

(1) The curative effect of erysipelas on malignant tumors is an established fact.

(2) The action on sarcoma is more powerful than on carcinoma, in about the ratio of 3 to 1.

(3) The treatment of inoperable malignant tumors by repeated inoculations of erysipelas is both practicable and not attended with great risk.

(4) The curative action is systemic, and probably due chiefly to the toxic products of the streptococcus, which products may be isolated and used without producing erysipelas.

(5) This method should *not be employed indiscriminately* until further experiments have proved its limitations.

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